

Serial No. 09/868,974

Amendments to the Claims

27. (previously presented) A shelf-stable solution formulation comprising a therapeutically effective amount of a glucagon-like peptide-1 (GLP-1) molecule which comprises the amino acid sequence:
- R_1 -X-Glu-Gly¹⁰-Thr-Phe-Thr-Ser-Asp¹⁵-Val-Ser-Ser-Tyr-Leu²⁰-Y-Gly-Gln-Ala-Ala²⁵-Lys-Z-Phe-Ile-Ala³⁰-Trp-Leu-Val-Lys-Gly³⁵-Arg- R_2 (SEQ ID NO:2)
- wherein R_1 is His or desamino-histidine, X is Ala, Gly or Val, Y is Glu or Gln, Z is Glu or Gln and R_2 is Gly-OH,
- and wherein said GLP-1 molecule further comprises one additional amino acid substitution; a pharmaceutically acceptable preservative; and a tonicity modifier,
- and wherein said formulation has a pH that is about 8.2 to about 8.8.
28. (previously presented) The formulation of claim 27 wherein the formulation has a pH that is about 8.2 to about 8.5.
29. (previously presented) The formulation of claim 27, wherein R_1 is L-histidine, X is Val, Y is Glu, Z is Glu, and R_2 is Gly-OH.
30. (previously presented) The formulation of claim 27 wherein the formulation is buffered by TRIS.
31. (cancelled)
32. (cancelled)
33. (previously presented) A method for treating diabetes comprising administering to a patient in need of such treatment an effective amount of the formulation of claim 27.
34. (previously presented) A shelf-stable solution formulation comprising a therapeutically effective amount of a glucagon-like peptide-1 (GLP-1) molecule selected from the group consisting of GLP-1(7-34), GLP-1(7-35), GLP-1(7-36), GLP-1(7-37), or the amide forms thereof, comprising at least one modification selected from the group consisting of:

Serial No. 09/868,974

- (a) substitution of a glycine, serine, cysteine, threonine, asparagine, glutamine, tyrosine, alanine, valine, isoleucine, leucine, methionine, phenylalanine, arginine, or D-lysine for lysine at position 26 and/or position 34 or substitution of a glycine, serine, cysteine, threonine, asparagine, glutamine, tyrosine, alanine, valine, isoleucine, leucine, methionine, phenylalanine, lysine, or a D-arginine for arginine at position 36;
- (b) substitution of an oxidation-resistant amino acid for tryptophan at position 31;
- (c) substitution of at least one of: tyrosine for valine at position 16; lysine for serine at position 18; aspartic acid for glutamic acid at position 21; serine for glycine at position 22; arginine for glutamine at position 23; arginine for alanine at position 24; and glutamine for lysine at position 26; and
- (d) substitution comprising at least one of: glycine, serine, or cysteine for alanine at position 8; aspartic acid, glycine, serine, cysteine, threonine, asparagine, glutamine, tyrosine, alanine, valine, isoleucine, leucine, methionine, or phenylalanine for glutamic acid at position 9; serine, cysteine, threonine, asparagine, glutamine, tyrosine, alanine, valine, isoleucine, leucine, methionine, or phenylalanine for glycine at position 10; and glutamic acid for aspartic acid at position 15;

a pharmaceutically acceptable preservative; and a tonicity modifier, wherein said formulation has a pH that is about 8.2 to about 8.8..

- 35. (previously presented) The formulation of claim 34 wherein the formulation has a pH that is about 8.2 to about 8.5.
- 36. (previously presented) The formulation of claim 34, wherein the GLP-1 molecule is selected from the group consisting of GLP-1(7-34), GLP-1(7-35), GLP-1(7-36), GLP-1(7-37), or the amide forms thereof, and provided that arginine is substituted for lysine at position 34.

Serial No. 09/868,974

37. (previously presented) The formulation of claim 34 wherein the formulation is buffered by TRIS.
38. (cancelled)
39. (cancelled)
40. (previously presented) A method for treating diabetes comprising administering to a patient in need of such treatment an effective amount of the formulation of claim 34.
41. (previously presented) A shelf-stable solution formulation comprising a therapeutically effective amount of a glucagon-like peptide-1 (GLP-1) molecule which comprises the amino acid sequence:
R₁-X-Glu-Gly¹⁰-Thr-Phe-Thr-Ser-Asp¹⁵-Val-Ser-Ser-Tyr-
Leu²⁰-Y-Gly-Gln-Ala-Ala²⁵-Lys-Z-Phe-Ile-Ala³⁰-Trp-Leu-Val-
Lys-Gly³⁵-Arg-R₂ (SEQ ID NO:2)
wherein R₁ is His or desamino-histidine, X is Ala, Gly or Val, Y is Glu or Gln, Z is Glu or Gln and R₂ is Gly-OH;
a pharmaceutically acceptable preservative; and a tonicity modifier,
wherein said formulation has a pH that is about 8.2 to about 8.8.
42. (previously presented) The formulation of claim 41 wherein the formulation has a pH that is about 8.2 to about 8.5.
43. (previously presented) The formulation of claim 41, wherein R₁ is L-histidine, X is Val, Y is Glu, Z is Glu, and R₂ is Gly-OH.
44. (previously presented) The formulation of claim 41 wherein the formulation is buffered by TRIS.
45. (cancelled)
46. (cancelled)
47. (previously presented) A method for treating diabetes comprising administering to a patient in need of such treatment an effective amount of the formulation of claim 41.